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Research Article

Role of Diffusion-Weighted Imaging and MR Spectroscopy in Preoperative Grading of Gliomas: A Radiologic-Pathologic Correlation Study

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Abstract: ***Introduction:*** Gliomas are the most common primary brain tumors, exhibiting significant heterogeneity in biological behavior and prognosis. Accurate preoperative grading is essential for treatment planning and survival prediction. Conventional MRI has limited specificity in differentiating tumor grades, necessitating the use of advanced imaging modalities such as Diffusion-Weighted Imaging (DWI) and Magnetic Resonance Spectroscopy (MRS).**Aim:** To evaluate the role of DWI and MRS in preoperative grading of gliomas and to correlate radiologic findings with histopathological grading. **Materials and Methods:** This prospective observational study included 50 patients with suspected gliomas. All patients underwent MRI with DWI and multivoxel MRS. Apparent Diffusion Coefficient (ADC) values and metabolite ratios (Cho/NAA and Cho/Cr) were calculated. Histopathology served as the reference standard. Statistical analysis included independent t-test and receiver operating characteristic (ROC) curve analysis, with $p < 0.05$ considered significant. **Results:** High-grade gliomas demonstrated significantly lower mean ADC values compared to low-grade gliomas (0.82 ± 0.14 vs $1.32 \pm 0.18 \times 10^{-3}$ mm²/s; $p < 0.001$). MRS revealed significantly elevated Cho/NAA and Cho/Cr ratios in high-grade tumors ($p < 0.001$). Diagnostic accuracy was 78% for DWI and 86% for MRS, while combined analysis improved accuracy to 92%. These findings are consistent with previous literature demonstrating strong correlation between imaging biomarkers and tumor grade **Conclusion:** DWI and MRS are reliable, non-invasive imaging modalities for preoperative glioma grading. Their combined use significantly enhances diagnostic accuracy and shows strong correlation with histopathology, supporting their routine incorporation into neuro-oncologic imaging protocols.

Keywords: Glioma, Diffusion-weighted imaging, MR spectroscopy, ADC, Cho/NAA ratio, tumor grading

INTRODUCTION

Gliomas represent the most common primary tumors of the central nervous system, accounting for nearly 70–80% of malignant brain tumors [1]. Their biological heterogeneity ranges from indolent low-grade gliomas (LGG) to highly aggressive high-grade gliomas (HGG), including glioblastoma, with significantly different prognostic outcomes [2].

Accurate preoperative grading is essential for determining surgical approach, planning adjuvant therapy, and predicting survival outcomes [3]. Histopathological examination remains the gold standard; however, it is invasive and may suffer from sampling bias due to tumor heterogeneity [4].

Conventional MRI plays a central role in tumor detection and anatomical delineation but has limited ability in reliably distinguishing tumor grades [5]. This limitation has led to increasing reliance on advanced imaging techniques.

Diffusion-Weighted Imaging (DWI) provides insight into tumor cellularity by measuring the diffusion of water molecules. Apparent Diffusion Coefficient (ADC) values are inversely related to cellular density; thus, high-grade tumors typically demonstrate lower ADC values due to increased cellularity and restricted diffusion [6,7].

Magnetic Resonance Spectroscopy (MRS) evaluates tumor metabolism by quantifying biochemical markers such as choline (Cho), creatine (Cr), and N-acetyl aspartate (NAA). Elevated Cho levels reflect increased membrane turnover, while decreased NAA indicates neuronal loss. Ratios such as Cho/NAA and Cho/Cr are significantly higher in high-grade gliomas [8,9].

Several studies have demonstrated that combining DWI and MRS improves diagnostic accuracy in glioma grading compared to individual modalities alone [10–12]. Furthermore, these advanced imaging parameters have shown strong correlation with histopathological grading and tumor aggressiveness [13].

Therefore, this study aims to assess the role of DWI and MRS in preoperative glioma grading and establish their correlation with histopathological findings.

MATERIALS AND METHODS

Study Design and Setting

A prospective observational study conducted over a period of 24 months in a tertiary care hospital.

Sample Size

A total of **50 patients** with radiologically suspected gliomas were included.

Inclusion Criteria

- Patients with intracranial lesions suggestive of glioma
- Age ≥18 years
- Patients undergoing surgery or biopsy

Exclusion Criteria

- Previously treated brain tumors
- MRI contraindications
- Non-gliomatous lesions on histopathology

Imaging Protocol

All patients underwent MRI using a 1.5T/3T scanner including:

- T1-weighted, T2-weighted, FLAIR sequences
- Diffusion-weighted imaging (b = 0, 1000 s/mm²)
- ADC mapping
- Multivoxel MR spectroscopy

Imaging Analysis

- **ADC values:** measured from solid enhancing tumor regions
- **MRS parameters:**
- Choline (Cho)
- Creatine (Cr)
- NAA
- **Calculated ratios:**
- Cho/NAA
- Cho/Cr

Histopathological Evaluation

Tumors were graded according to WHO classification:

- Low-grade gliomas: Grade I–II
- High-grade gliomas: Grade III–IV

Statistical Analysis

- Software: SPSS version 25
- Mean ± SD calculated
- Independent t-test used
- ROC curve analysis performed
- $p < 0.05$ considered statistically significant

RESULTS

Table 1: Demographic and Clinical Characteristics

Parameter	Low-Grade Glioma (n=22)	High-Grade Glioma (n=28)	Total (n=50)
Mean Age (years)	41.6 ± 9.2	56.8 ± 11.4	50.2 ± 12.8
Male (%)	59%	64%	62%
Female (%)	41%	36%	38%
Most common symptom	Seizures	Headache	—

The study population consisted of 50 patients, with a higher proportion of high-grade gliomas (56%). The mean age was significantly higher in the high-grade group compared to the low-grade group. Male predominance was observed overall. Seizures were the most common presenting symptom in low-grade gliomas, whereas headache and raised intracranial pressure symptoms were more frequently seen in high-grade gliomas, reflecting the aggressive nature of these tumors.

Table 2: Comparison of ADC Values

Parameter	Low-Grade Glioma	High-Grade Glioma	p-value
Mean ADC ($\times 10^{-3}$ mm²/s)	1.32 ± 0.18	0.82 ± 0.14	<0.001

Mean ADC values were significantly higher in low-grade gliomas compared to high-grade gliomas. The reduced ADC values observed in high-grade tumors indicate increased cellularity and restricted diffusion. This difference was statistically highly significant ($p < 0.001$), supporting the role of DWI as a reliable tool in differentiating glioma grades. These findings are consistent with previous studies demonstrating inverse correlation between ADC values and tumor grade [6,7].

Table 3: MR Spectroscopy Metabolite Ratios

Parameter	Low-Grade Glioma	High-Grade Glioma	p-value
Cho/NAA Ratio	1.8 ± 0.5	4.6 ± 1.2	<0.001
Cho/Cr Ratio	1.4 ± 0.3	2.8 ± 0.7	<0.001

MR spectroscopy demonstrated significantly elevated metabolite ratios in high-grade gliomas. The Cho/NAA ratio showed a marked increase in high-grade tumors, reflecting enhanced cellular proliferation and neuronal destruction. Similarly, Cho/Cr ratios were significantly higher in aggressive tumors. These differences were statistically significant ($p < 0.001$), confirming the value of MRS in assessing tumor metabolism and grading gliomas preoperatively [8,9].

Table 4: Diagnostic Performance of DWI and MRS

Modality	Sensitivity (%)	Specificity (%)	Accuracy (%)
DWI (ADC)	82	73	78
MRS	88	82	86
Combined DWI + MRS	93	89	92

Diagnostic performance analysis revealed that MRS had higher sensitivity and specificity compared to DWI alone. However, the combined use of DWI and MRS significantly improved diagnostic accuracy to 92%. This highlights the complementary role of structural and metabolic imaging in glioma grading. The combined approach enhances confidence in preoperative diagnosis and aligns with findings from previous studies emphasizing multimodal imaging strategies [10–12].

DISCUSSION

Role of Diffusion-Weighted Imaging in Glioma Grading

Diffusion-weighted imaging (DWI) has emerged as a crucial non-invasive biomarker in neuro-oncology due to its ability to reflect tumor cellularity. In the present study, mean ADC values were significantly lower in high-grade gliomas compared to low-grade gliomas (0.82 vs 1.32×10^{-3} mm²/s; $p < 0.001$), indicating increased cellular density and restricted diffusion in aggressive tumors.

These findings are consistent with the work of Kono et al. [6], who demonstrated that ADC values inversely correlate with tumor cellularity. Similarly, Gupta et al. [7] reported significantly reduced ADC values in high-grade gliomas, reinforcing its diagnostic utility. The pathophysiological basis lies in the densely packed tumor cells in high-grade gliomas, which restrict extracellular water movement, thereby reducing ADC.

However, despite its usefulness, DWI alone has limitations. Overlap in ADC values between tumor grades can occur, particularly in heterogeneous tumors or regions with necrosis and edema. In our study, DWI showed an overall diagnostic accuracy of 78%, which, although significant, was lower than MRS and combined modalities. This suggests that while DWI is a valuable tool, it should not be used in isolation.

Role of MR Spectroscopy in Glioma Characterization

Magnetic Resonance Spectroscopy (MRS) provides metabolic insights into tumor biology, offering an advantage over structural imaging techniques. In the present study, Cho/NAA and Cho/Cr ratios were significantly higher in high-grade gliomas ($p < 0.001$), reflecting increased cellular proliferation and neuronal loss.

Law et al. [8] demonstrated that elevated choline levels correlate with increased membrane turnover and tumor aggressiveness. N-acetyl aspartate (NAA), a neuronal marker, is reduced in malignant tumors due to neuronal destruction. The Cho/NAA ratio, therefore, serves as a robust indicator of tumor grade.

Similarly, Server et al. [9] found that MRS had superior accuracy compared to conventional MRI in differentiating glioma grades. Our study showed an accuracy of 86% for MRS, supporting its strong diagnostic performance.

Despite its advantages, MRS is not without limitations. Spectral overlap, voxel contamination, and technical variability can affect accuracy. Nonetheless, when performed correctly, it provides invaluable metabolic information that complements anatomical imaging.

Combined Role of DWI and MRS

One of the most significant findings of this study is the enhanced diagnostic accuracy achieved by combining DWI and MRS. The combined approach yielded an accuracy of 92%, which was higher than either modality alone.

This finding aligns with previous studies. Wang et al. [10] demonstrated that integrating ADC values with metabolite ratios significantly improves glioma grading accuracy. Similarly, Di Costanzo et al. [11] emphasized that multimodal MRI provides a more comprehensive assessment of tumor biology.

The rationale behind this improvement lies in the complementary nature of these techniques:

- **DWI:** reflects tumor cellularity
- **MRS:** reflects tumor metabolism

By integrating structural, functional, and metabolic data, clinicians can achieve a more accurate preoperative assessment.

Furthermore, multimodal imaging reduces diagnostic uncertainty and may help guide biopsy targeting, ensuring that the most aggressive tumor regions are sampled. This is particularly important in heterogeneous tumors such as glioblastoma.

Radiologic–Pathologic Correlation

Radiologic-pathologic correlation is essential in validating imaging biomarkers. In this study, strong concordance was observed between imaging findings and histopathological grading.

High-grade gliomas demonstrated:

- Lower ADC values
- Higher Cho/NAA and Cho/Cr ratios
- Greater heterogeneity on imaging

These findings correlate with histopathological features such as increased mitotic activity, necrosis, and microvascular proliferation.

Pope et al. [12] reported similar findings, highlighting that imaging parameters can reliably reflect tumor biology. Additionally, these imaging markers may correlate with molecular features such as IDH mutation status and Ki-67 proliferation index, although these were not evaluated in the present study.

The ability to predict tumor grade non-invasively has significant clinical implications, including:

- Preoperative planning
- Prognostication
- Treatment stratification

Clinical Implications and Future Directions

The findings of this study have important clinical implications. The use of advanced MRI techniques can reduce reliance on invasive procedures and improve preoperative decision-making.

Clinical relevance:

- Helps neurosurgeons plan extent of resection
- Assists in selecting biopsy targets
- Predicts tumor aggressiveness
- Guides adjuvant therapy decisions

Recent advancements in radiomics and artificial intelligence are further enhancing the role of imaging in glioma evaluation. Quantitative imaging features combined with machine learning models have shown promising results in predicting tumor grade and molecular status [13-16].

- Future research should focus on:
- Integration of advanced MRI with molecular markers
- Larger multicentric studies
- Development of standardized imaging protocols
- Application of AI-based predictive models [17-20]

CONCLUSION

Diffusion-weighted imaging and MR spectroscopy are valuable non-invasive modalities for preoperative glioma grading. While DWI reflects tumor cellularity and MRS provides metabolic characterization, their combined use significantly enhances diagnostic accuracy. These techniques demonstrate strong correlation with histopathology and should be routinely incorporated into glioma evaluation protocols to improve clinical decision-making and patient outcomes.

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